Translation

PCT/JP2003/013855

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| | | |
|---|---|---|
| Applicant's or agent's file reference<br>PH-1885-PCT | **FOR FURTHER ACTION** | See Form PCT/IPEA/416 |
| International application No.<br>PCT/JP2003/013855 | International filing date (*day/month/year*)<br>29 October 2003 (29.10.2003) | Priority date (*day/month/year*)<br>29 October 2002 (29.10.2002) |
| International Patent Classification (IPC) or national classification and IPC<br>C12N 15/09, A01K 67/027, C12N 5/10 | | |
| Applicant<br>ORIENTAL YEAST CO., LTD. | | |

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☒ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) 1 diskette , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

| | |
|---|---|
| Date of submission of the demand<br>02 April 2004 (02.04.2004) | Date of completion of this report<br>28 July 2004 (28.07.2004) |
| Name and mailing address of the IPEA/JP<br><br>Facsimile No. | Authorized officer<br><br>Telephone No. |

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2003/013855

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP 03/13855

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 3, 5, 6, 8-12, 17, 18, 22, 23 | YES |
| | Claims | 1, 2, 4, 7, 13-16, 19-21, 24, 25 | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1-25 | NO |
| Industrial applicability (IA) | Claims | 1-25 | YES |
| | Claims | | NO |

2. Citations and explanations

Document 1: H. XIA et al., "siRNA-mediated Gene Silencing In Vitro and In Vivo," Nat. Biotechnol., October 2002, Vol. 20, No. 10, pp. 1006-1010, (Epub 16 September 2002)

Document 2: Y. HUANG et al., "Role of Polyadenylation in Nucleocytoplasmic Transport of mRNA," Mol. Cell. Biol., 1996, Vol. 16, pp. 1534-1542

Document 3: L. MCKENDRICK et al., "Interaction of Eukaryotic Translation Initiation Factor 4G with the Nuclear Cap-binding Complex Provides a Link Between Nuclear and Cytoplasmic Functions of the m(7) Guanosine Cap," Mol. Cell Biol., June 2001, Vol. 21, No. 11, pp. 3632-3641

Document 4: M. YONAHA et al., "Transcriptional Termination and Coupled Polyadenylation In Vitro," EMBO J., 2000, Vol. 19, pp. 3770-3777

Document 5: Database GenBank, Accession No. AF435852, 12 November 2001, Definition: Mus Musculus Ski Proto-oncogene (Ski) mRNA, Complete Cds.,

Document 6: Y. ZHENG et al., "RNA interference in Human Cells is Restricted to the Cytoplasm," RNA, July 2002, Vol. 8, No. 7, pp. 855-860

Document 7: Y. Lee et al., "The Nuclear RNase III Drosha Initiates microRNA Processing," Nature, 25 September 2003, Vol. 425, No. 6956, pp. 415-419

Document 8: I. PAPP, et al., "Evidence for Nuclear Processing of Plant Micro RNA and Short Interfering RNA Precursors," Plant Physiol., July 2003, Vol. 132, No. 3, pp. 1382-1390

Claims 1, 2, 4, 7, 13-16, 19-21, 24 and 25

Document 1 presents a double stranded RNA expression vector wherein the sequence which codes double-stranded RNA (ds-RNA) with a hairpin RNA structure, which is to say a system loop structure, is located immediately after the transcriptional start site for the polymerase II promoter from the cytomegalovirus (CMV), and a poly A sequence, which is to say a sequence that stops the RNA polymerase, is located on the 3' side. In addition, document 1 indicates that the double stranded RNA expression vector in question has been injected into the tails or the brains of mice. Consequently, the inventions that are set forth in the abovementioned claims are the same as the inventions that are presented in document 1; therefore, they lack novelty.

Claims 3 and 4

A person skilled in the art could choose to substitute CMV early gene promoters that were well known to a person skilled in the art prior to the priority date of the present application for the polymerase II promoter from CMV which is disclosed in document 1 in order to accommodate the expression period or the like of the gene to be knocked down, as appropriate. In addition, the invention that is set forth in the abovementioned claims cannot be considered to exhibit any especially prominent

effect as a result of the configuration in question. Consequently, the invention that is set forth in the abovementioned claims does not involve an inventive step in the light of the disclosures of document 1 and the abovementioned well-known technology.

Claims 5 and 6

It would be easy for a person skilled in the art to conceive of introducing an autocatalytic RNA-cleaving ribosome into a vector in the light of the disclosures of document 2, and the invention that is set forth in the abovementioned claims cannot be considered to exhibit any especially prominent effect as a result of the configuration in question. Consequently, the invention that is set forth in the abovementioned claims does not involve an inventive step in the light of the disclosures of documents 1 and 2.

Claim 8

Document 4 presents the MAZ domain, and it cannot be considered to be especially difficult to substitute the MAZ domain for the poly A sequence; therefore, the invention that is set forth in the abovementioned claim does not involve an inventive step in the light of the disclosures of documents 1 and 4.

Claim 9

With consideration of common technical knowledge prior to the priority date of the present application, a person skilled in the art could have determined the base sequence that codes the loop region, as necessary, and the invention that is set forth in the abovementioned claim cannot be considered to exhibit any especially prominent effect as a result of the configuration in question. Consequently, the invention that is set forth in the

abovementioned claim does not involve an inventive step in the light of the disclosures of document 1 and common technical knowledge prior to the priority date of the present application.

Claims 10-12, 17, 18, 22 and 23

It would be easy for a person skilled in the art to conceive of targeting disease-related genes by means of ds-RNA, and there is not seen to be any significant difficulty in employing the Ski gene indicated in prior art citation 5, which was well known prior to the priority date for the present application as presented in the GenBank database, for that purpose. In addition, the inventions that are set forth in the abovementioned claims cannot be considered to exhibit any especially prominent effect as a result of the configuration in question; consequently, the inventions that are set forth in the abovementioned claims do not involve an inventive step in the light of the disclosures of document 1 and prior art citation 5.

Furthermore, documents 7 and 8, which were published after the priority date of the present application, indicate the existence of proteins that act in a similar manner to Dicer within the nucleus. That being said, prior to the priority date of the present application it is considered to have been impossible for a person skilled in the art to foresee that it would be possible to induce RNA interference without translocating the cytoplasm by introducing ds-RNA into the nucleus. However, the scope of the inventions that are set forth in the claims is not limited only to inventions wherein transcribed ds-RNA is introduced into the nucleus; therefore, the abovementioned opinions have been appended.